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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte INGRID HENRIKSEN, TORE OMTVEIT, VERA KASPARKOVA, and ANNE KJERSTI FAHLVIK

Appeal 2008-6236
Application 10/071,505
Technology Center 1600

Decided:[1] January 30, 2009

Before RICHARD M. LEBOVITZ, FRANCISCO C. PRATS, and MELANIE L. McCOLLUM, *Administrative Patent Judges*.

LEBOVITZ, *Administrative Patent Judge*.

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[1] The two-month time period for filing an appeal or commencing a civil action, as recited in 37 CFR § 1.304, begins to run from the decided date shown on this page of the decision. The time period does not run from the Mail Date (paper delivery) or Notification Date (electronic delivery).

DECISION ON APPEAL

This is a decision on appeal from the final rejection of claims 1, 3, 5-7, 11, 12, and 19. Jurisdiction is under 35 U.S.C. § 6(b). We reverse the rejection.

STATEMENT OF THE CASE

The claims are drawn to a method of administering a gas-containing contrast agent to a subject. The method involves admixing a contrast agent and a flushing medium and then administering the admixed product to a subject over an infusion period of 5-60 minutes. According to the Specification, the prior art administered contrast agents as a bolus over short periods of 5-20 seconds (Spec. 2:4-14). The Specification discloses that continuous infusion of the contrast agent over periods from 1 minute to 60 minutes minimizes "diagnostic artefacts [sic] such as shadowing and . . . lengthen[s] the useful time window for imaging beyond the relatively short duration of the backscatter signal peak resulting from passage of a contrast agent bolus" (*id.* at 2:18-22). The Specification also teaches that using a vertically positioned delivery vessel, such as a syringe, and an admixture of contrast and flushing agents, improves homogeneity and delivery of the contrast agent (Spec. 3:24 to 4:27).

Claims 1, 3, 5-7, 11, 12, and 19 are pending. Appellants appeal from the Examiner's final rejection of claims 1, 3, 5-7, 11, 12, and 19 under 35 U.S.C. § 103(a) as obvious in view of Unger et al. (US 6,033,645, Mar. 7, 2000) (Ans. 3). We select claim 1 as representative. Because Appellants do not separately argue the patentability of the claims, claims 3, 5-7, 11, 12, and

19 stand or fall with claim 1. 37 C.F.R. § 41.37(c)(vii)(1). Claim 1 reads as follows:

> 1. A method of administering a gas-containing contrast agent to a subject by continuous infusion, the improvement comprising enhancing product homogeneity by controllably delivering said gas-containing contrast agent from an upper extremity of an essentially vertically positioned syringe and admixing with a flushing medium prior to administration to the subject, delivering the admixed product to the subject over an infusion period of 5-60 minutes.

PRINCIPLES OF LAW

"During [patent] examination, the examiner bears the initial burden of establishing a *prima facie* case of obviousness." *In re Kumar*, 418 F.3d 1361, 1366 (Fed. Cir. 2005).

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains.

35 U.S.C. § 103(a) (2004).

> Although common sense directs one to look with care at a patent application that claims as innovation the combination of two known devices according to their established functions, it can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does. This is so because inventions in most, if not all, instances rely upon building blocks long since uncovered, and claimed discoveries almost of necessity will be combinations of what, in some sense, is already known.

KSR Int'l Co. v. Teleflex Inc., 550 U.S. 398, ___, 127 S. Ct. 1727, 1741 (2007).

> [T]he ultimate determination of obviousness "does not require absolute predictability of success. ... [A]ll that is required is a reasonable expectation of success." *In re O'Farrell*, 853 F.2d 894, 903-904 (Fed. Cir. 1988); *see also In re Longi*, 759 F.2d 887, 897(Fed. Cir. 1985).

Brown & Williamson Tobacco Corp. v. Philip Morris Inc., 229 F.3d 1120, 1125 (Fed. Cir. 2000).

"[W]hen the PTO shows sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." *In re Spada*, 911 F.2d 705, 708 (Fed. Cir. 1990).

ISSUE

Does Unger describe or suggest "delivering" an "admixed product" of a contrast agent and flushing medium to a subject "over an infusion period of 5-10 minutes" as recited in claim 1?

FINDINGS OF FACT (FF)

Scope and content of the prior art

1. Unger describes gas filled vesicles which can serve as contrast agents in diagnostic imaging techniques, such as ultrasound, computed tomography, and magnetic resonance imaging (Unger, at col. 6, ll. 49-57; Ans. 3).

2. Unger states that, when the vesicles are administered to a subject via injection, they pool or accumulate near the injection site (*id*. at col. 47, ll. 64-65).

3. Unger states: "To promote the transport of the . . . vesicle composition from the injection site into the bloodstream and, thereafter, to the region of interest, a flush may be administered" (*id.* at col. 47, l. 65 to col. 48, l. 1).

4. "The flush may act, generally by mechanical action, to 'push' or 'wash' the injected compositions into the bloodstream" (*id.* at col. 48, ll. 1-3).

5. According to Unger,

> the rate at which the lipid and/or vesicle compositions are administered to a patient may have a profound effect on the quality of the resulting diagnostic image. Specifically, it has been found that the occurrence of diagnostic artifacts in diagnostic images may be directly related to the rate at which the lipid and/or vesicle compositions are administered. Thus, as discussed above, the administration of a lipid and/or vesicle composition at too high a rate can result in an excess concentration of lipid and/or vesicle composition at the region of interest. . . Conversely, the administration of a lipid and/or vesicle composition at too low a rate can result in an insufficient concentration of lipid and/or vesicle composition at the region of interest. In the case of ultrasound imaging involving, for example, gas filled vesicles, the application of energy (sound waves) can result in too little sound energy being reflected, thereby resulting, for example, in inadequate contrast in the resulting ultrasound image.

(*Id.* at col. 44, ll. 40-60.)

6. Figure 1 of Unger shows a schematic representation of a system for administering a contrast agent comprising a syringe **14** containing a contrast agent and a mechanical injector **22** comprising a flush agent (*id.* at col. 49, ll. 38-53). Unger's Figure 2 shows a similar system with a syringe **14'** containing a contrast agent and a mechanical injector **22'**. The "flush agent" of Unger corresponds to the "flushing medium" of claim 1. *See also* Ans. 10-11.

7. The syringe **14** and injector **22** are in flow contact with each other via a conduit **26** which is adapted to administer the contrast agent and flush agent to a patient (*id.* at col. 49, ll. 53-58; *see* Fig. 1). *See also* Ans. 10-11.

8. According to Unger

> The flush agent **24'** is desirably administered after ejection of the contrast agent **20'**. This generally involves operation of the control means **42'** to drive the mechanical injector **22'**. As with the embodiment discussed above, the control means **42'** controls the amount of power supplied to the mechanical injector **22'** and permits regulation of the rate at which the mechanical injector **22'** operates and, thereby, the rate at which the flush agent **24'** is ejected from the mechanical injector **22'**. The flush agent **24'** is ejected from the mechanical injector **22'** and into and through the tubing **30'** and the port **44**. The flush agent **24'** serves to push or drive the contrast agent **20** from its location in the port **44** and/or the tubing **30'**, throughout the length of the tubing **30'**, and into the patient. . . . The flush may be stopped after contrast agent **20'** has been administered to the patient. Alternatively, the flush may be continued so that the flush agent **24'** is also injected into the patient. The rate at which the mechanical injector **22'** is operated may be varied at any time during the ejection of the flush agent **24'**, as desired.

(*Id.* at col. 51, ll. 35-56; as quoted on pages 10-11 of the Answer.)

9. Unger teaches several examples of administration periods for contrast agent and flush followed by ultrasound imaging ((*id.* at col. 52, ll. 3-7):

Example 2: 2 second injection with contrast agent and 2 second flush (*id.* at col. 52, l. 41-45). Unger describes the ultrasound image produced by this regime as inferior (*id.* at col. 52, ll. 51-55).

Example 3: 5-10 second injection with contrast agent and 10-15 second flush (*id.* at col. 52, ll. 59-64). The image is described as "very robust and long-lasting" (*id.* at col. 52, ll. 66-67).

Example 4: 15 second injection with contrast agent and 10-15 second flush (*id.* at col. 53, ll. 1-6). The image is described as "less robust" than Example 3 (*id.* at col. 53, ll. 8-9).

Example 9 (prophetic): 50 second injection with contrast agent and 5-10 minute flush (*id.* at col. 53, ll. 54-58).

Level of ordinary skill in the art

10. Persons of ordinary skill in the art had the technical skill to determine the effective dosages and infusion periods over which to administer effective dosages of contrast and flushing agent (*id.* at col. 44, l. 61 to col. 45, l. 53; col. 45, l. 65 to col. 47, l. 21; Ans. 4-5).

ANALYSIS

The Examiner has the burden of establishing prima facie obviousness of the claimed subject matter. *In re Kumar,* 418 F.3d at 1366. To meet this burden, a reason must be provided as to why the differences between the prior art and the claimed invention would have been obvious to persons of ordinary skill in the art. 35 U.S.C. § 103(a) (2004); *See KSR*, 127 S. Ct. at 1741.

In this case, the Examiner contends that Unger describes the claimed method of administering a gas-containing contrast agent by continuous infusion, but does not "explicitly" teach the limitation of "delivering the admixed product" of contrast agent and flushing medium "over an infusion period of 5-60 minutes" as required by claim 1 (*see* Ans. 4). However, the Examiner asserts that the claimed infusion period would have been arrived at routinely when optimizing for "volume of the composition, gaseous vesicles, type of encapsulation and other patient variable[s] such as age, area of

interest, etc." (*id.*). In reaching this conclusion, the Examiner provided evidence from Unger that it was within the level of ordinary skill in the art to determine the effective dosages and infusion periods over which to administer effective dosages of contrast and flushing agent (FF10). The Examiner also relied on Unger's disclosure at column 51, lines 35-56 (FF8), to meet the claimed limitation of "admixing" the contrast agent and flushing agent prior to administration to the subject (*see* Ans. 10).

The Examiner has not met the burden of establishing prima facie obviousness of the claimed subject matter. Claim 1 recites that an "admixed product" of "contrast agent" and "flushing medium" is administered "over an infusion period of 5-60 minutes." The Examiner has not provided adequate evidence that Unger's disclosure would have suggested to persons of ordinary skill in the art administration of an admixture comprising the agent and flush for the claimed infusion period.

While Unger discloses that administration periods are routinely determinable (FF10), in its examples, the contrast agent is administered from about 2 to 50 seconds which is substantially less than the claimed infusion period of 5-60 minutes (FF9). The Examiner contends that the claimed period would have been arrived at by routine optimization taking into account the factors ordinarily relied upon the skilled worker (Ans. 4; FF10). However, the evidence of record militates against this conclusion.

Unger explicitly teaches that the rate of administration of the contrast agent (gas filled vesicles) has "a profound effect on the quality of the resulting diagnostic image" (FF5). Delivery at "too high a rate can result in an excess of concentration" of the contrast agent "at the region of interest" (*id.*). Delivery "at too low a rate can result in an insufficient concentration

of lipid and/or vesicle composition at the region of interest" (*id.*). Consistently, in the examples, Unger states that the image quality is low when 2 and 15 second administration periods are utilized (FF9; Examples 2 and 4), but "very robust and long-lasting" for a 5-10 second intermediate injection period (FF9; Example 3). While obviousness does not require absolute predictability of success, there must be a reasonable expectation of success. *Brown*, 229 F.3d at 1125. With teachings that (1) contrast agent administration rate has a "profound" effect on image quality and (2) working examples in which contrast agent is administered over seconds, not minutes, the evidence does not support the Examiner's position that it would have been routine to vary contrast agent administration time several-fold in excess over what is disclosed by Unger, and in doing so, there would have been a reasonable expectation of success.

The Examiner also contends that Unger teaches admixing contrast agent and flushing medium, relying on column 51, lines 35 to 56 of Unger for this disclosure. Unger, in fact, teaches that the flush agent "serves to push or drive the contrast agent" from the port or tubing and into the patient (FF8; *see also* FF2-4). The flush is "administered after ejection of the contrast agent" (FF8). While it may be correct that admixing occurs between the contrast and flush agents, there is no explicit teaching in Unger that this result takes place when the flush agent pushes the contrast agent into the patient. Thus, the Examiner's position appears to be that admixing *inherently* takes place during Unger's administration method. When a rejection is based on inherency, the Examiner must provide a "sound basis" for believing that the prior art accomplishes the same result which is claimed. *See In re Spada*, 911 F.2d at 708.

Here, the Examiner has not explained how Unger's method would result in administration of an admixture of contrast agent and flush agent for an infusion period of 5-60 minutes as required by claim 1. The longest infusion period explicitly described in Unger appears in Example 9 when a 50 second injection with contrast agent is followed by a 5-10 minute flush (FF9; Unger, at col. 53, ll. 54-58). Even were an admixture to occur between the contrast and flush agents as the latter was pushing the former into the patient, the Examiner has not provided a sound basis for believing that the admixture would be continuously administered for at least 5 minutes of the flush period, a necessary condition to satisfy claim 1. Once the contrast agent is pushed into the patient, the Examiner has not articulated a reason for believing that portions of it would remain in Unger's tube or port admixing with the flush medium as it is administered to the patient for 5 minutes.

CONCLUSION OF LAW

Unger does not describe or suggest "delivering" an "admixed product" of a contrast agent and flushing medium to a subject "over an infusion period of 5-10 minutes" as recited in claim 1. We reverse the rejection of claim 1 and dependent claims 3, 5-7, 11, 12, and 19 which incorporate all the limitations of claim 1.

REVERSED

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